

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

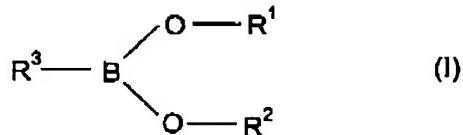
CLAIM LISTING

What is claimed is:

1. (Currently amended) A method of:
 - a) inhibiting the lipolytic activity of hormone-sensitive lipase against triacylglycerols, diacylglycerols, cholesterol acyl esters or steroid acyl esters; and/or
 - b) modulating the plasma level of free fatty acids, glycerol, LDL-cholesterol, HDL-cholesterol, insulin and/or glucose; and/or
 - c) modulating intracellular triacylglycerol and cholesterol ester stores, intracellular level of fatty acids, fatty acid esters, diacylglycerols, phosphatidic acids, long chain acyl-CoA's as well as citrate or malonyl-CoA; and/or
 - d) increasing insulin sensitivity in adipose tissue, skeletal muscle, liver or pancreatic β cells; and/or
 - e) modulating insulin secretion from pancreatic β cells; and/or
 - f) inhibiting male fertility

in a patient comprising, administering to a patient in need of such method a therapeutically effective amount of a boronic acid, an ester thereof, a prodrug thereof,

wherein the boronic acid, an ester thereof or a prodrug thereof is of the general formula I



wherein R¹ and R² are independently selected from hydrogen, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, **phosphinyl**, **selenyl**, **germyl**, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, **phosphinyl**, **selenyl**, **germyl**, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

alkynyl, aryl, heteroaryl, C₃₋₈-heterocycll and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycll and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycll and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycll and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycll and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycll and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycll and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycll and C₃₋₁₀-cycloalkyl;

wherein R² is optionally covalently bound to R¹ by one or two ether, thioether, B, O-B, C-C, C=C or C-N bonds, to form a ring system with the O-atoms to which R¹ and R² are bound, said ring system may optionally form a fused ring system with benzene; and

R³ is selected from C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycll and C₃₋₁₀-cycloalkyl, wherein each of C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycll and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen,

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, thioxo, amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl.

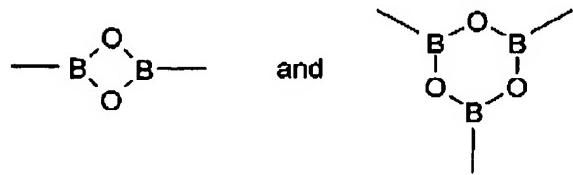
Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

phosphinyl, selenyl, germethyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl;
or any tautomeric forms, stereoisomers, mixture of stereoisomers, racemic mixture, oligomers or polymorphs,
or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof.

2. (Previously presented) The method according to claim 1, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 2.0 and 11.5.

3. (Original) The method according to claim 1, wherein the boronic acid, an ester thereof or a prodrug thereof is a dimer or trimer of a boronic acid.

4. (Currently amended) The method according to claim 3, wherein said dimer or trimer of the boronic acid comprises a structure selected from:

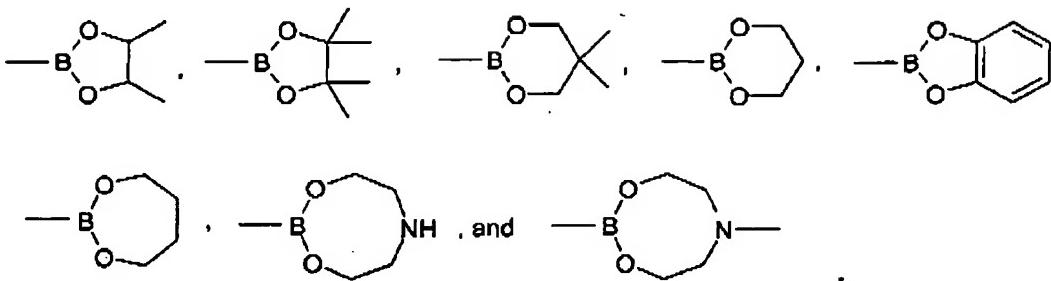


5. (Original) The method according to claim 1, wherein the boronic acid, an ester thereof or a prodrug thereof comprises an atom selected from the group consisting of S, P, I, Br, Si, Se and Ge.

6. Cancelled)

7. (Currently amended) The method according to claim 1, wherein the boronic acid, an ester thereof, or a prodrug thereof, comprises a structure selected from the group consisting of

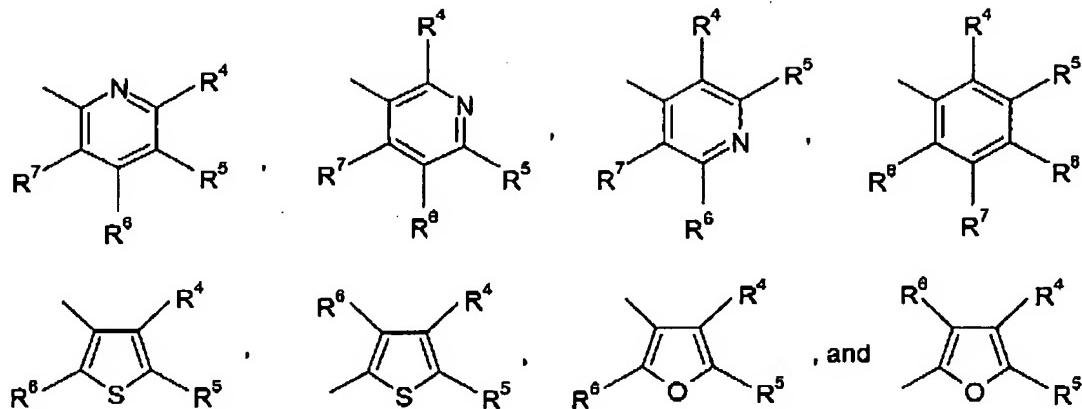
Attorney Docket No. 6413.204-US
 Ebdrup et al.
 Serial No. 10/614,233 Filed July 7, 2003



8. (Previously presented) The method according to claim 1, wherein the group R³ in the general formula (I) comprises an optionally substituted moiety selected from the group consisting of pyrrolidine-2-yl, pyrrolidine-3-yl, pyrrole-2-yl, pyrrole-3-yl, 3H-pyrrole-2-yl, 3H-pyrrole-3-yl, 3H-pyrrole-4-yl, 3H-pyrrole-5-yl, oxolane-2-yl, oxolane-3-yl, furane-2-yl, furane-3-yl, thiolane-2-yl, thiolane-3-yl, thiophene-2-yl, thiophene-3-yl, pyrazole-3-yl, pyrazole-4-yl, pyrazole-5-yl, pyrazolidine-3-yl, pyrazolidine-4-yl, imidazole-2-yl, imidazole-4-yl, imidazole-5-yl, imidazolidine-2-yl, imidazolidine-4-yl, 3H-pyrazole-3-yl, 3H-pyrazole-4-yl, 3H-pyrazole-5-yl, isoxazole-3-yl, isoxazole-4-yl, isoxazole-5-yl, oxazole-2-yl, oxazole-4-yl, oxazole-5-yl, isothiazole-3-yl, isothiazole-4-yl, isothiazole-5-yl, thiazole-2-yl, thiazole-4-yl, thiazole-5-yl, 1,2,5-oxadiazole-3-yl, 1,3,5-oxadiazole-2-yl, 1,3,5-oxadiazole-4-yl, 1,3,4-oxadiazole-2-yl, 1,2,3,5-oxatriazole-4-yl, 1,2,5-thiadiazole-3-yl, 1,3,5-thiadiazole-2-yl, 1,3,5-thiadiazole-4-yl, 1,3,4-thiadiazole-2-yl, 1,2,3,5-thatriazole-4-yl, 1,2,3-triazole-4-yl, 1,2,3-triazole-5-yl, 1,2,4-triazole-3-yl, 1,2,4-triazole-5-yl, 1,2,5-triazole-3-yl, tetrazole-5-yl, 1,3-oxathiole-2-yl, 1,3-oxathiole-4-yl, 1,3-oxathiole-5-yl, benzofurane-2-yl, benzofurane-3-yl, isobenzofurane-1-yl, benzothiophene-2-yl, benzothiophene-3-yl, isobenzothiophene-1-yl, 1H-indole-2-yl, 1H-indole-3-yl, 2H-isoindole-1-yl, indolizine-1-yl, indolizine-2-yl, indolizine-3-yl, 1H-benzimidazole-2-yl, 1H-benzothiazole-2-yl, 1H-benzoxazole-2-yl, 1H-benzisoxazole-3-yl, 3H-indazole-3-yl, piperidine-1-yl, piperidine-2-yl, piperidine-3-yl, piperidine-4-yl, piperazine-1-yl, piperazine-2-yl, 2,5-dione-piparazine-1-yl, 2,5-dione-piparazine-3-yl and phenyl.

9. (Currently amended) The method according to claim 1, wherein the group R³ is selected from the group consisting of:

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003



wherein R⁴, R⁵, R⁶, R⁷ and R⁸ are independently selected from C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, thioxo, amino, imino, cyano, nitro, silyl, boranyl, **phosphinyl, selenyl, germyl**, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, **phosphinyl, selenyl, germyl**, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, **phosphinyl, selenyl, germyl**, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, **phosphinyl, selenyl, germyl**, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, **phosphinyl, selenyl, germyl**, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, **phosphinyl, selenyl, germyl**, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, **phosphinyl, selenyl, germyl**, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocyclyl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl,

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycl and C₃₋₁₀-cycloalkyl, wherein each of hydroxy, sulfanyl, sulfonyl, sulfinyl, amino, imino, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycl and C₃₋₁₀-cycloalkyl is optionally substituted with one or more substituents independently selected from hydroxy, sulfanyl, sulfonyl, sulfinyl, oxo, thioxo, halogen, amino, imino, cyano, nitro, silyl, boranyl, phosphinyl, selenyl, germyl, C₁₋₆-alkyl, C₂₋₆-alkenyl, C₂₋₆-alkynyl, aryl, heteroaryl, C₃₋₈-heterocycl and C₃₋₁₀-cycloalkyl.

10. (Previously presented) The method according to claim 9, wherein the molar weight of each of R⁴, R⁵, R⁶, R⁷ and R⁸ is below about 100 Dalton.

11. (Original) The method according to claim 9, wherein R⁴, R⁵, R⁶, R⁷ and R⁸ are independently selected from hydrogen, halogen, hydroxyl, perhalomethyl, perhalomethoxy, C₁₋₆-alkyl, C₁₋₆-alkoxy and C₁₋₆-alkylthio.

12. (Original) The method according to claim 9, wherein R⁴, R⁵, R⁶, R⁷ and R⁸ are independently selected from hydrogen, halogen, methyl, methoxy, thiomethoxy, perhalomethyl, perhalomethoxy

13. (Original) The method according to claim 9, wherein R⁴, R⁵, R⁶, R⁷ and R⁸ are independently selected from hydrogen, halogen, trifluoromethyl and trifluoromethoxy.

14. (Previously presented) The method according to claim 1, wherein the group R¹ is H.

15. (Previously presented) The method according to claim 1, wherein the group R¹ is H and the group R² is H.

16. (Previously presented) The method according to claim 1, wherein said boronic acid, an ester thereof or a prodrug thereof is selected from the group consisting of:
2-(5-Chlorothiophen-2-yl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane,
2-(5-Chlorothiophen-2-yl)-5,5-dimethyl-[1,3,2]dioxaborinane,

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

2-(5-Chlorothiophen-2-yl)-[1,3,6,2]dioxazaborocane,
2-(3,5-Difluorophenyl)-[1,3,6,2]dioxazaborocane,
2-(3-Bromophenyl)-[1,3,6,2]dioxazaborocane,
2-(3-Chlorophenyl)-[1,3,6,2]dioxazaborocane,
2-(3-Fluorophenyl)-[1,3,6,2]dioxazaborocane,
2-(3-Trifluoromethylphenyl)-[1,3,6,2]dioxazaborocane,
2-(3,4,5-Trifluorophenyl)-[1,3,6,2]dioxazaborocane,
2-(3-Chlorophenyl)-5,5-dimethyl-[1,3,2]dioxaborinane,
5,5-Dimethyl-2-(3-trifluoromethylphenyl)-[1,3,2]dioxaborinane,
2-(5-Chloro-2-methoxyphenyl)-[1,3,6,2]dioxazaborocane,
2-(3-Trifluoromethoxyphenyl)-[1,3,6,2]dioxazaborocane,
2-(3,5-Dichlorophenyl)-[1,3,6,2]dioxazaborocane,
2-(3-Chloro-4-fluorophenyl)-[1,3,6,2]dioxazaborocane,
2-(4-Methylthiophen-2-yl)-[1,3,6,2]dioxazaborocane,
2-(3-Bromophenyl)-5,5-dimethyl-[1,3,2]dioxaborinane,
2-(5-Chloro-2-methoxyphenyl)-5,5-dimethyl-[1,3,2]dioxaborinane,
5,5-Dimethyl-2-(3,4,5-trifluorophenyl)-[1,3,2]dioxaborinane,
5,5-Dimethyl-2-(3-trifluoromethoxyphenyl)-[1,3,2]dioxaborinane,
2-(3,5-Dichlorophenyl)-5,5-dimethyl-[1,3,2]dioxaborinane,
2-(3-Chloro-4-fluorophenyl)-5,5-dimethyl-[1,3,2]dioxaborinane,
2-(3-Fluorophenyl)-5,5-dimethyl-[1,3,2]dioxaborinane,
5,5-Dimethyl-2-(4-methylthiophen-2-yl)-[1,3,2]dioxaborinane,
2-(3-Bromophenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane,
2-(5-Chloro-2-methoxyphenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane,
4,4,5,5-Tetramethyl-2-(3-trifluoromethoxyphenyl)-[1,3,2]dioxaborolane,
2-(3,5-Dichlorophenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane,
2-(3-Chloro-4-fluorophenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane,
2-(3-Chlorophenyl)-4,4,5,5-tetramethyl-[1,3,2]dioxaborolane,
4,4,5,5-Tetramethyl-2-(3-trifluoromethylphenyl)-[1,3,2]dioxaborolane,
4,4,5,5-Tetramethyl-2-(4-methylthiophen-2-yl)-[1,3,2]dioxaborolane,
4-Benzylxyloxyphenylboronic acid,
4-Bromobenzeneboronic acid n-methyldiethanolamine cyclic ester,
2-(3,5-Difluorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane,3-Bromobenzeneboronic acid n-methyldiethanolamine cyclic ester,
2-(4-Bromophenyl)-5,5-dimethyl-1,3,2-dioxaborinane,
2-(2-Chlorophenyl)-5,5-dimethyl-1,3,2-dioxaborinane,
2-(5,5-Dimethyl-[1,3,2]dioxaborinan-2-yl)-benzonitrile,
2-(2-Fluoro-phenyl)-5,5-dimethyl-[1,3,2]dioxaborinane,
5-Chloro-2-methoxyphenylboronic acid,
3,5-Dibromophenylboronic acid,
3-Ethoxyphenylboronic acid,
3-phenylphenylboronic acid,
4-fluorophenylboronic acid,
2-Bromophenylboronic acid,
3-Bromophenylboronic acid,
2,6-Dichlorophenylboronic acid,
3-Methylphenylboronic acid,
2-Chlorophenylboronic acid,

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

3-Chlorophenylboronic acid,
3-(Trifluoromethoxy)benzeneboronic acid,
3-Trifluoromethylphenylboronic acid,
3,5-Bis(Trifluoromethyl)phenylboronic acid,
3,5-Dichlorophenylboronic acid,
3-Chloro-4-fluorophenylboronic acid,
3,5-Difluorophenylboronic acid,
3-Fluorophenylboronic acid,
2,3-Difluoro-4-pentylphenylboronic acid,
(3-Dluoro-4-benzyloxyphenyl)boronic acid,
3,4,5-Trifluorophenylboronic acid,
2,3,5-Trichlorophenylboronic acid,
2,5-Dichlorophenylboronic acid,
2,3-Difluorophenylboronic acid,
2,5-Difluorophenylboronic acid,
4'-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)acetanilide,
3,4-Difluorophenylboronic acid,
2,3-Dichlorophenylboronic acid,
2,3-Difluoro-4-bromophenylboronic acid,
3-Fluoro-4-phenylboronic acid,
2-Methoxy-5-fluorophenylboronic acid,
3,4-Dichlorophenylboronic acid,
5-Indolyl boronic acid,
3-Formylphenylboronic acid,
6-Methoxy-2-phenyl-hexahydro-pyrano[3,2-a][1,3,2]dioxaborinane-7,8-diol,
3'-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2-trimethylsilylthiophen,
4'-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)2-nitrothiophene,
1-Benzothiophen-3-ylboronic acid,
2-Formyl-3-thiopheneboronic acid,
2-Thien-3-yl-1,3,2-benzodioxaborole,
3-Thiophenboronic acid,
2-(2-Formyl-3-methylthien-5-yl)-1,3,2-dioxaborinane,
4-Methylthiophene-2-boronic acid,
5-Methylfuran-2-boronic acid,
5-Methylthiophene-2-boronic acid,
Benz[b]furan-2-boronic acid,
Benz[B]thiophene-2-boronic acid,
Furan-2-boronic acid,
5-Chlorothiophene-2-boronic acid,
5-Cyanothiophene-2-boronic acid,
5-Acetylthiophene-2-boronic acid,
Thiophene-2-boronic acid,
3-Bromo-2-thiophene-2-boronic acid, and
5,5-Dimethyl-2-(3-iodothiophen-2-yl)-[1,3,2]dioxaborinane.

17. (Previously presented) The method according to claim 6, wherein the compound is R³-B(OH)₂ and the pK_a of the R³ substituent is between 2.0 and 11.5.

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

18. (Original) The method according to claim 1, wherein said boronic acid, or an ester thereof or a prodrug thereof has a molar weight of no greater than 1000 D.

19. (Previously presented) The method according to claim 1, wherein the molar weight of said boronic acid, an ester thereof or a prodrug thereof is less than 750 D.

20. (Previously presented) The method according to claim 1, wherein said boronic acid, an ester thereof or a prodrug thereof has an IC₅₀ value as determined by the assay 3190.2 or 3180.1 disclosed herein of less than 50 μM.

21. (Previously presented) The method according to claim 1, wherein said boronic acid, an ester thereof or a prodrug thereof has a solubility in water at 25 °C and pH 2.0 of at least 0.5 mg/L.

22. (Original) The method according to claim 1, wherein administration of said boronic acid, an ester thereof or a prodrug thereof is by the oral, nasal, transdermal, pulmonal, or parenteral route.

23. (Previously presented) The method according to claim 1, wherein a pharmaceutical composition is administered, said pharmaceutical composition comprising, as an active ingredient, said boronic acid, said ester thereof, said prodrug thereof, or a pharmaceutically acceptable salt thereof, or a pharmaceutically acceptable solvate thereof, together with a pharmaceutically acceptable carrier or diluent.

24. (Previously presented) The method according to claim 2, wherein a pharmaceutical composition is administered, said pharmaceutical composition comprising, as an active ingredient, said boronic acid, said ester thereof or said prodrug thereof, or a pharmaceutically acceptable salt thereof, together with a pharmaceutically acceptable carrier or diluent.

25. (Previously presented) The method according to claim 24 wherein the pharmaceutical composition in unit dosage form, comprising from about 0.05 mg to about 2000 mg, preferably from about 0.1 to about 500 mg of the boronic acid, an ester thereof, a prodrug

Attorney Docket No. 6413.204-US
Fbdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

thereof or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof.

26. (Previously presented) The method according to claim 23 wherein the pharmaceutical composition is for oral, nasal, transdermal, pulmonal or parenteral administration.

27. (Original) A method according to claim 1 for treating a disorder where it is desirable to inhibit the lipolytic activity of hormone-sensitive lipase against triacylglycerols, diacylglycerols, cholesterol acyl esters or steroid acyl esters.

28. (Original) A method according to claim 1 for treating a disorder where it is desirable to modulate the plasma level of free fatty acids or to modulate the handling, storage and oxidation of intracellular fatty acid and cholesterol.

29. (Original) The method according to claim 27, wherein said disorder is selected from the group consisting of insulin resistance, diabetes type 1, diabetes type 2, metabolic syndrome X, impaired glucose tolerance, hyperglycemia, dyslipidemia, obesity, abnormalities of lipoprotein metabolism and any combination thereof.

30. (Original) The method according to claim 28, wherein said disorder is selected from the group consisting of insulin resistance, diabetes type 1, diabetes type 2, metabolic syndrome X, impaired glucose tolerance, hyperglycemia, dyslipidemia, obesity, abnormalities of lipoprotein metabolism and any combination thereof.

31. (Currently amended) A method of treating insulin resistance, diabetes type 1, diabetes type 2, metabolic syndrome X, impaired glucose tolerance, hyperglycemia, dyslipidemia, hyperlipoproteinemia, hypertriglyceridemia, hyperlipidemia, hypercholesterolemia, or other abnormalities of lipoprotein metabolism, said method comprising administering to a patient in need thereof a pharmaceutically effective amount of a boronic acid according to claim 1, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof.

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

32. (Previously presented) The method according to claim 31, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 2.0 and 11.5.

33. (Original) The method according to claim 27, wherein the patient is treated with said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof for at least about 1 week, for at least about 2 weeks, for at least about 4 weeks, for at least about 2 months or for at least about 4 months.

34. (Original) The method according to claim 28, wherein the patient is treated with said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof for at least about 1 week, for at least about 2 weeks, for at least about 4 weeks, for at least about 2 months or for at least about 4 months.

35. (Original) The method according to claim 31, wherein the patient is treated with said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof for at least about 1 week, for at least about 2 weeks, for at least about 4 weeks, for at least about 2 months or for at least about 4 months.

36. (Previously presented) The method according to claim 2, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 3.0 and 10.5.

37. (Previously presented) The method according to claim 2, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 4.0 and 9.5.

38. (Previously presented) The method according to claim 2, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 5.0 and 8.5.

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

39. (Previously presented) The method according to claim 2, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 5.5 to 8.0.

40. (Previously presented) The method according to claim 2, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 6.0 to 7.5.

41. (Previously presented) The method according to claim 10, wherein the molar weight of each of R⁴, R⁵, R⁶, R⁷ and R⁸ is below about 80 Dalton.

42. (Previously presented) The method according to claim 10, wherein the molar weight of each of R⁴, R⁵, R⁶, R⁷ and R⁸ is below 50 Dalton.

43. (Previously presented) The method according to claim 10, wherein the molar weight of each of R⁴, R⁵, R⁶, R⁷ and R⁸ is below about 20 Dalton.

44. (Previously presented) The method according to claim 17, wherein the compound is R³-B(OH)₂ and the pK_a of the R³ substituent is between 3.0 and 10.5.

45. (Previously presented) The method according to claim 17, wherein the compound is R³-B(OH)₂ and the pK_a of the R³ substituent is between 4.0 and 9.5.

46. (Previously presented) The method according to claim 17, wherein the compound is R³-B(OH)₂ and the pK_a of the R³ substituent is between 5.0 and 8.5.

47. (Previously presented) The method according to claim 17, wherein the compound is R³-B(OH)₂ and the pK_a of the R³ substituent is between 5.5 to 8.0.

48. (Previously presented) The method according to claim 17, wherein the compound is R³-B(OH)₂ and the pK_a of the R³ substituent is between 6.0 to 7.5.

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

49. (Previously presented) The method according to claim 19, wherein the molar weight of said boronic acid, an ester thereof or a prodrug thereof is less than 500 D.

50. (Previously presented) The method according to claim 19, wherein the molar weight of said boronic acid, an ester thereof or a prodrug thereof is less than 350 D.

51. (Previously presented) The method according to claim 19, wherein the molar weight of said boronic acid, an ester thereof or a prodrug thereof is less than 300 D.

52. (Previously presented) The method according to claim 19, wherein the molar weight of said boronic acid, an ester thereof or a prodrug thereof is less than 250 D.

53. (Previously presented) The method according to claim 19, wherein the molar weight of said boronic acid, an ester thereof or a prodrug thereof is less than 200 D.

54. (Previously presented) The method according to claim 20, wherein said boronic acid, an ester thereof or a prodrug thereof has an IC₅₀ value as determined by the assay 3190.2 or 3180.1 disclosed herein of less than 5 μM.

55. (Previously presented) The method according to claim 20, wherein said boronic acid, an ester thereof or a prodrug thereof has an IC₅₀ value as determined by the assay 3190.2 or 3180.1 disclosed herein of less 500 nM.

56. (Previously presented) The method according to claim 20, wherein said boronic acid, an ester thereof or a prodrug thereof has an IC₅₀ value as determined by the assay 3190.2 or 3180.1 disclosed herein of less than 100 nM.

57. (Previously presented) The method according to claim 21, wherein said boronic acid, an ester thereof or a prodrug thereof has a solubility in water at 25 °C and pH 2.0 of at least 2.5 mg/L.

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

58. (Previously presented) The method according to claim 21, wherein said boronic acid, an ester thereof or a prodrug thereof has a solubility in water at 25 °C and pH 2.0 of at least 20 mg/L.

59. (Previously presented) The method according to claim 21, wherein said boronic acid, an ester thereof or a prodrug thereof has a solubility in water at 25 °C and pH 2.0 of at least 200 mg/L.

60. (Previously presented) The method according to claim 21, wherein said boronic acid, an ester thereof or a prodrug thereof has a solubility in water at 25 °C and pH 2.0 of at least 2 g/L.

61. (Previously presented) The method according to claim 25 wherein the pharmaceutical composition in unit dosage form, comprising from about 0.1 to about 500 mg of the boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof or a pharmaceutically acceptable solvate thereof.

62. (Previously presented) The method according to claim 32, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 3.0 and 10.5.

63. (Previously presented) The method according to claim 32, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 4.0 and 9.5.

64. (Previously presented) The method according to claim 32, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 5.0 and 8.5.

65. (Previously presented) The method according to claim 32, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 5.5 to 8.0.

Attorney Docket No. 6413.204-US
Ebdrup et al.
Serial No. 10/614,233 Filed July 7, 2003

66. (Previously presented) The method according to claim 32, wherein the pK_a of said boronic acid, an ester thereof, a prodrug thereof or a pharmaceutically acceptable salt thereof is between 6.0 to 7.5.